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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/775,879	02/02/2001	Sunghwa Choe	2225-0003	3956

20855 7590 04/24/2002

ROBINS & PASTERNAK LLP
545 MIDDLEFIELD ROAD
SUITE 180
MENLO PARK, CA 94025

EXAMINER

BAUM, STUART F

ART UNIT	PAPER NUMBER
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1638

12

DATE MAILED: 04/24/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/775,879	Applicant(s) CHOE ET AL.	
	Examiner Stuart Baum	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-35 is/are pending in the application.
- 4a) Of the above claim(s) 6,7,9,11,13,15,17,19,21 and 23-35 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-5,8,10,12,14,16,18,20 and 22 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
 If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
 * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
 a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). ____ |
| 2) <input checked="" type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____ | 6) <input type="checkbox"/> Other: |

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Applicant's election without traverse of Group I, claims 1-5, 8, 10, 12, 14, 16, 18, 20, and 22 including SEQ ID NO's:20 and 21 in Paper No. 11 is acknowledged.

Objection is made to claims 1-5 which specifies a DNA sequence by referring to Figures 8A-8D. 37 CFR 1.821(d) requires the use of the assigned sequence identifier (e.g. SEQ I.D. NO: #) in all instances where the description or claims of a patent application discuss sequences.

Drawings

The drawings are objected to for the reasons indicated on the enclosed form PTO-948. Correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 8, 10, 12, 14, 16, 18, 20, and 22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The inventors claim an isolated *dwarf7* (*dwf7*) polynucleotide that imparts at least one *dwf7* mutant phenotype when expressed in a plant, said polynucleotide selected from the group consisting of: a polynucleotide comprising the nucleotide sequence depicted at positions 143 to 322 of SEQ ID NO:20, a polynucleotide comprising the nucleotide sequence depicted at

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positions 143 to 1552, a polynucleotide having at least 70% identity with the above sequences, a fragment of the above sequences comprising at least 15 contiguous nucleotides and complements thereof.

The Applicants originally identified the monogenic recessive *dwf7-1* mutant from a screen of 14,000 T-DNA transformed lines of *Arabidopsis*. The characteristic *dwf7-1* phenotype includes, short robust stems, reduced fertility and dark-green, round and curled leaves. The *dwf7-1* mutation was found to be allelic to the *ste1* mutant which was previously shown to encode a delta 7 sterol C-5 desaturase.

The Applicants do not identify structural features unique to the *Arabidopsis dwf7* mutant protein, the functional domains of the protein nor the overall function of the protein. The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. Given the lack of description for the *Arabidopsis dwf7* mutant protein, it remains unclear what features identify a *Arabidopsis dwf7* mutant protein, including a *Arabidopsis dwf7* mutant gene with 70% homology to SEQ ID NO:20 or sequences comprising at least 15 contiguous nucleotides of SEQ ID NO:20. Since a *Arabidopsis dwf7* mutant protein has not been described by specific structural features or by specific function, the specification fails to provide an adequate written description to support the generic claims.

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Claims 1-5, 8, 10, 12, 14, 16, 18, 20, and 22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1-5, 8, 10, 12, 14, 16, 18, 20, and 22 are broadly drawn an isolated *dwarf7* (*dwf7*) polynucleotide that imparts at least one *dwf7* mutant phenotype when expressed in a plant, said polynucleotide selected from the group consisting of: a polynucleotide comprising the nucleotide sequence depicted at positions 143 to 322 of SEQ ID NO:20, a polynucleotide comprising the nucleotide sequence depicted at positions 143 to 1552, a polynucleotide having at least 70% identity with the above sequences, a fragment of the above sequences comprising at least 15 contiguous nucleotides and complements thereof wherein transforming a plant with any of the above sequences will alter the sterol composition of plants relative to a wild-type plant. Said transformed plants will have either less cholesterol or an increased amount of cholesterol compared to wild-type plants.

The Applicants have not taught how to use their invention. They have only described the cloning and characterization of the nucleic acid sequence. In particular, they have described the phenotype of the *dwf7* mutant and have asserted that transforming a plant with SEQ ID NO:20 or fragment as described above will produce a plant exhibiting the described phenotype. It has not been taught how transforming a plant with an above mentioned sequence will produce a dominant phenotype, or produce a plant with either increased or decreased levels of cholesterol relative to wild-type plants, especially using a sequence with only 70% identity to SEQ ID NO:20 or a fragment comprising at least 15 contiguous nucleotides of SEQ ID NO:20. It has not

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been taught how transforming a plant with the before mentioned sequences will over-ride or knockout the wild-type allele.

It cannot be predicted by one of skill in the art that nucleic acids that have 70% identity to SEQ IN NO:20 or comprise a fragment comprising at least 15 contiguous nucleotides of SEQ ID NO:20 will produce a polypeptide with the same activity as a *dwf7* polypeptide of SEQ ID NO:20. Bowie et al (1990, Science 247:1306-10) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of the protein to fold into unique three-dimensional structures that allows it to function and carry out the instructions of the genome. The cited reference also teaches that the prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex (pg 1306, left column). Bowie et al teach that while it is known that many amino acid substitutions are possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or none at all (pg 1306, right column). The sensitivity of proteins to alterations in even a single amino acid in a sequence is exemplified by Burgess et al (1990, J. Cell Biol. 111:2129-2138), who teach that the replacement of a single lysine residue at position 118 of acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein.

In addition, Napier et al (1999, Current Opinion in Plant Biology 2(2):123-127) teach identifying desaturases by sequence homology does not always yield predictable results. A

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sunflower desaturase was identified by comparison to a borage delta-6 fatty acid desaturase. The homology between the sunflower protein and the borage delta-6 desaturase was 65% identity at the amino acid level—however, the enzymatic activity of the two proteins was found to be different. “Thus although the sunflower protein appeared to encode a fatty acid desaturase, it was only after functional characterization that the true identity and substrate of the enzyme became clear” (page 126, right column, 1st full paragraph).

Hamada et al (1998, Plant Physiology 118:591-598) teach that expressing heterologous desaturases in plants does not always give predictable results. Hamada et al overexpressed a tobacco microsomal ω -3 fatty acid desaturase cDNA (NtFAD3) under the control of a mosaic constitutive promoter that confers about 10-fold higher levels of constitutive expression than the CaMV 35S promoter. The results of overexpression in tobacco plants resulted in a 40% increase in alpha-linolenic acid in roots and only a 10% increase in leaves (abstract and page 593, right column, 1st paragraph of results). These results suggest that endogenous factors contribute to the observed result that can not be predicted a priori.

Due to the unpredictable nature of plant transformation, one of skill in the art can not reasonably generate transformed plants with a desired phenotype using a specific isolated gene. Levels of transgene expression in plants are generally unpredictable and vary between independent transformants; this variability is usually explained by differences in transgene copy number and/or integration site (Finnegan and McElroy, 1994. Bio/technology 12: 883-888 pg. 883 2nd paragraph).

Given the unpredictability of identifying a desaturase based on sequence homology alone and the unpredictability of producing a plant with an increased or decreased amount of

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cholesterol as stated above; given the lack of working examples of producing a plant with an increased or decreased amount of cholesterol, given the lack of guidance in the specification for producing a plant with an increased or decreased amount of cholesterol using a delta-7 sterol C-5 desaturase or any one of the multitude of sequences that fall under 70% identical or a fragment comprised of 15 contiguous nucleotides for the reasons given above, it would require undue experimentation by one skilled in the art to practice the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 8, 10, 12, 14, 16, 18, 20, and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Husselstein et al (1999, Plant Molecular Biology 39:891-906).

The Applicants broadly claim an isolated *dwf7* polynucleotide that imparts at least one *dwf7* mutant phenotype when expressed in a plant, said polynucleotide selected from the group consisting of: a polynucleotide comprising the nucleotide sequence depicted at positions 143-322 of SEQ ID NO:20, a polynucleotide comprising the nucleotide sequence depicted at positions 143 to 1552 of SEQ ID NO:20, a polynucleotide comprising a nucleotide sequence having at least 70% identity to the above sequences, and a fragment comprising at least 15 contiguous nucleotides of the above sequences.

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Husselstein et al teach a nucleic acid sequence that encodes a delta-7 sterol C-5 desaturase from *Arabidopsis*, and exhibits 99.3% identity with SEQ ID NO:20 and 100% identity to a polynucleotide comprising the nucleotide sequence depicted at positions 143-322 and 100% identity to a fragment comprising at least 15 contiguous nucleotides, including a recombinant vector comprising a before mentioned nucleic acid (page 895), host cell transformed with recombinant vector (page 895), method of producing a DWF7 polypeptide (page 896), a transgenic plant comprising said recombinant vector (page 900) a method of altering sterol composition of a plant (page 901), and a method of producing less cholesterol relative to a wild-type plant (page 902) and as such anticipates the Applicants invention.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart Baum whose telephone number is (703) 305-6997. The examiner can normally be reached on Monday-Friday 8:30AM – 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 or (703) 305-3014 for regular communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the legal analyst, Kim Davis, whose telephone number is (703) 305-3015.

Stuart Baum Ph.D.

April 18, 2002

ELIZABETH F. McELWAIN
PRIMARY EXAMINER
GROUP 1800

Elizabeth F. McElwain